Subacute dementia as presenting feature of carcinomatous leptomeningeal metastases

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Demenzia subaguda como cuadro de presentación de carcinomatosis meníngea

La carcinomatosis leptomeningea constituye una seria complicación de los tumores sólidos y hemato-ológicos extraneurales y ocasional en las neoplasias primarias del sistema nervioso y que cuenta con una mediana de supervivencia inferior a 6 meses. El cáncer de mama, pulmón y gástrico así como el melanoma, el linfoma y la leucemia son las neoplasias más comunes implicadas en la invasión leptomeningea. Esta complicación se presenta con síntomas y signos sugestivos de alteración de pares craneales. El líquido cefalorraquídeo (LCR) normalmente presenta pleocitosis, aumento de las proteínas e hipoglucorraquia. Los hallazgos típicos de la resonancia magnética nuclear consisten en incrementos focales de la captación de gadolinio. Finalmente el diagnóstico se confirma mediante el examen patológico del LCR.

CASE REPORT

We report a case of a 77 years old woman with a history of hypertension and hysterectomy for a benign ovarian tumor two years ago. During the last two months she had developed a progressive deterioration of the memory for recent events with apraxia and disorientation. Also, she became unable to manage for basic activities. Previously to admission, she started with headache, nausea and vomiting. Her physical examination showed poor memory, flat affect and incongruous animo. Neurologic examination didn’t reveal other abnormalities. Her blood test and cultures were rigorously normal with the exception of carcinembryonic antigen (CEA) and Ca 15.3 levels (144.2 and 40.6). Neurospecific enolase, α-F and Ca 125 were normal. Thyroid hormones levels were within normal limits and $B_{12}$ levels. Serologic studies for citomegalovirus (CMV), herpes simplex virus (HSV), human immunodeficiency virus (HIV), borreia, syphilis and M. pneumoniae obtained negative results. Psychiatric exams did not show functional diseases as depression, anxiety or psychosis. Contrast-enhanced computed tomography of the head revealed a very dilated ventricular system, with temporal and frontal horns alterations. There was a low density around front horn suggesting a mild transpendymal trasudation of CSF. Cortical grooves were scarce for her age. In addition, a number of contrast-enhanced images arising from the bone inner surface hinting a leptomeningeal origin were found. Magnetic resonance imaging (MRI) showed a diffuse enhanced meningeal gadolinium uptake. CSF analysis was consistent with leptomeningeal invasion: hypoglycorrachia (0.36 g/l (0.45-0.8)), pleocytosis (WBC count of 20 3/mm$^3$) and increased protein levels (454 100-400). Immunoglobulins, albumina and their ratio were normal. CSF β2-microglobulin was augmented (1,711 0-1,500) but this parameter was normal in plasma, so the CSF/plasma ratio resulted high. Cytology yielded large malignant and pleomorphic cells with enlarged nuclei, occasional nucleoli, and coarse chromatin, all these findings suggestive of meningeal metastases. Body-scan disclosed an isolated 1.5 cm-2 cm node in the posterior segment of the right upper lobe with a atelectasia. Enlarged mediastinal lymph nodes were not found. At this time, paliative CNS irradiation were administered. Some days later, patient was moved to a Paliative Care Hospital where she had a respiratory sepsis. She did not response to intense antibiotherapy and died 15 days later.

DISCUSSION

The most common originating sites of tumors producing carcinomatous meningitis are breast and lung$^{1-5}$. It is estimated that 1%-5% of patients with metastases...
tic breast cancer experience carcinomatous meningitis in the absence of parenchymal brain disease and in 0% of patients with secondary central nervous system involvement. It has been reported that, two thirds of the patients with carcinomatous meningitis have features of lobular histologic type in their primary tumors. Patients with carcinomatous leptomeningeal metastases usually develop multiple cranial neuropathies, patchy radiculopathies or mental status changes. The most frequent presenting findings are meningeal irritation (mainly headache) and cranial nerve palsies affecting to the extracranial muscles. Also, multipleplex mononeuropathies, raised intracranial pressure, cerebellar dysfunction, epilepsy, lower motor neuron spinal nerve lesions, confusion and cortical dysfunction are common. Dementia seems to be a rather unusual presenting symptom and to our knowledge, no other cases have been published before. Our first differential diagnoses to be ruled out was Alzheimer’s dementia. The patient met all criteria for this disease: memory deterioration, disphasia, apraxia and impairment in cognitive and social abilities without oscillation in the level of consciousness. However, the diagnosis of Alzheimer disease can only be established if other organic causes of dementia have been previously excluded. Another dementia causes were: Creutzfeld-Jacob disease, syphilis, HIV infection, virous meningoencephalitis; metabolic infectious: Creuzfeld-Jacob disease, syphilis, HIV established if other organic causes of dementia have not been included. In our patient the aformentioned abnormalities. We can conclude that our patient suffered dementia due to an hydrocephalus resulting in blockage of CSF flow that small lession would be very exceptional that producing above. Also abnormal CSF flow is common in patients with leptomeningeal cancer. Several groups have documented normal ventricular CSF kinetics using radionucleid ventriculography with Iridium 111 and Technetium-99m-DTPA. These abnormalities in the cerebrospinal flow are associated with poor terapeutic responses to intrathecal chemotherapy due to restricted access of the drug to the tumor, and with treatment-related toxicity derived from high local drug concentrations. Once the subaracnoid space is infiltrated by tumor cells, widespread involvement of the leptomeninges ensues. Consequently, intrathecal chemotherapy is the mainstay of treatment. Notwithstanding systemic drugs may occasionally also be beneficial. Radiotherapy is usually reserved for areas of bulk or symptomatic leptomeningeal disease. The preferred route for delivery of intrathecal chemotherapy is through an Omaya reservoir. There are some drugs used for this purpose as methotrexate, thiopeta, cytarabine and sustained-release cytarabine. In summary, the treatment of meningitis carcinomatous is not curative and patient survival is usually less than 6 months. Radiation therapy and intrathecal chemotherapy can offer palliation by arresting neurologic progression in clinically stable patients. Some authors suggest that patients with a poor performance status (KP <70) should be treated symptomatically and those with a good KP should receive more aggressive treatment. Herein we report an exceptional presenting symptom of leptomeningeal carcinomatosis: subacute dementia. Although the lung lesion was not biopsied, given her neurologic deficits and functional status one possibility was lung as primary localization. However that small lesion would be very exceptional that produce leptomeningeal metastases.

Key words: leptomeningeal carcinomatosis, subacute dementia.

References